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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1636	20

DATE MAILED: 08/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/042,775	GATTI ET AL.	
	Examiner	Art Unit	
	Maria B Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7,9-19 and 21-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-7,9-19 and 21-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This office action is in response to an amendment filed 6/2/03, Paper No. 7. Claims 4, 8 and 20 have been canceled and claims 23-27 have been added. Claims 1-2, 10, 14, 17 and 18 have been amended. Claims 1-3, 5-7, 9-19 and 21-27 are pending. Receipt of a substitute oath for David Rawlings is acknowledged. New grounds of rejection are made herein and therefore this action is not final.

Response to Amendment

Rejection of claims 1, 2, 6, 12-13, 17, 19 and 21-22 under 35 U.S.C. 102(e) as being anticipated by Kastan et al. US 6,387,640 B1 is withdrawn in light of amendments to claims. Specifically, the claims have been amended to recite that the mammalian cell that is infected with the viral vector encoding ATM is ATM deficient.

Rejection of claim 4 under 35 U.S.C. 112, first paragraph, is withdrawn in light of cancellation of claim 4.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 6 and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kastan et al. US 6,387,640 B1 (see entire document) in view of Rappold et al. JCB Vol 153(3), pp 613-620, (see entire document). **This is a new rejection.**

Applicants claim a method for recombinant production of functional ataxia-telangiectasis (ATM) protein by infecting ATM-deficient mammalian cells with a viral vector encoding ATM.

Kastan et al. teach vectors for the cloning and expression of ATM kinase or FLAG-tagged ATM kinase (column 19, line 32-35). A wide variety of promoters are contemplated (e.g. column 20, line 1-23). Preferred vectors are viral vectors such as vaccinia (column 20, line 25-29). Methods for expression of ATM *in vivo* in a cell are provided (e.g. column 28, line 25-32 or column 30, line 56-column 31, line 33). FLAG tag is utilized for immunoprecipitation of ATM with M2 monoclonal antibody following transfection of 293T cells with a cloned chimeric FLAG-ATM gene (column 31, line 2-22). Kastan et al. teach that tumor cells such as MCF7 and RKO cells represent an example of a mammalian expression cells that can be used for functional assays of ATM activity (column 19, line 63-67). Kastan et al. do not teach use of ATM deficient cells for ATM expression.

Rappold et al teach that an examination of ATM function is hampered in wild-type cells (page 615, column 1, paragraph 2). They further teach that to examine the effects of radiation on cells, they must use ATM deficient cells. Specifically, they use a fibroblast cell line that is devoid of ATM called FT169A (page 615, column 1, paragraph 3). In these experiments, FT169A cells express no ATM until reconstituted with wild-type ATM cDNA, YZ5 (e.g. Figure 3A).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the tumor cells taught by Rappold et al. with the ATM deficient cells taught by Rappold et al. because Antelman et al. teach that it is within the ordinary skill of the art to express recombinant ATM in a cell and because Rappold et al. teach that it is within the ordinary skill of the art to use an ATM deficient cell as a host cell for expression. One would have been motivated to do so in order to receive the expected benefit of unhampered comparison of functional assays involving the analysis of ATM kinase activity. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1-2, 6, 15, 17, 19 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kastan et al. US 6,387,640 B1 (see entire document) in view of Zhang et al. PNAS 94, pp 8021-8026, (see entire document). **This is a new rejection.**

Applicants claim a method for recombinant production of functional ataxia-telangiectasis (ATM) protein by infecting ATM-deficient mammalian cells with a viral vector encoding ataxia-telangiectasia protein and isolating with anti-ATM antibody.

Kastan et al. teach expression vectors for expression of ATM kinase or Flag tagged ATM kinase (column 19, line 32-35). A wide variety of promoters are contemplated (e.g. column 20, line 1-23). Preferred vectors are viral vectors such as vaccinia (column 20, line 25-29). Methods for expression of ATM in vivo in a cell are provided (e.g. column 28, line 25-32 or column 30, line 56-column 31, line 33). FLAG tag is utilized for immunoprecipitation of ATM with M2

monoclonal antibody following transfection of 293T cells with a cloned ATM gene (column 31, line 2-22). Kastan et al. teach that tumor cells such as MCF7 and RKO cells represent an example of a mammalian expression cells that can be used for functional assays of ATM activity (column 19, line 63-67). Kastan et al. do not teach infection of ATM deficient cells nor does Kastan et al. teach use of anti-ATM for isolation of ATM.

Zhang et al teach expression of ATM in ATM deficient cells to avoid isolation of endogenous ATM (e.g. page 8023, column 2). Three anti-ATM antibodies were used to isolate ATM in AT1ABR and AT3ABR cells which express no endogenous ATM (e.g. Figure 2). ATM was expressed from an EBV based vector to complement radiosensitive phenotypes in these cells and assay kinase activity (e.g. Figure 5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the tumor cells and the FLAG antibody taught by Kastan et al. with the ATM deficient cells and anti-ATM antibodies taught by Zhang et al. because Kastan et al. teach that it is within the ordinary skill of the art to express recombinant ATM in a cell and isolate it with anti-FLAG and because Rappold et al. teach that it is within the ordinary skill of the art to use an ATM deficient cell as a host cell for expression and to isolate ATM with anti-ATM. One would have been motivated to do so in order to receive the expected benefit of detection of any endogenous ATM in the cell by use of anti-ATM and not FLAG that detects recombinant ATM and the avoidance of isolation of endogenous ATM by use of an ATM deficient cell line. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth t5he best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-7, 9-19 and 21-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection.**

Applicant's claims read on a recombinant viral vector comprising a genus of ATM genes.

Applicant's claims read on a genus of functional ATM proteins.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus. In the instant case, applicants do not disclose the claimed gene but disclose full-length human ATM cDNA (GenBank Accession No. U33841). The genomic version of the recited genes is not disclosed in the specification. While the human ATM cDNA is known, the entire gene has not been disclosed. All of the components of the gene such as regulation sequences, introns, and exons must be determined empirically in order to generate the ATM gene without any disclosure about

its structure. The skilled artisan would not conclude that applicant was in possession of viral vector comprising the claimed gene.

In the instant case, applicants have only disclosed an ATM protein encoded by the full-length human cDNA Genbank accession number U33841 (page 8). Proteins encoded by ATM genes could be products of allelic variations or fragmentations or members of the family of kinases that includes ATM. Furthermore, ATM has numerous functions and yet the specification does not disclose the functions that are considered essential and hence are essential elements of the inventions. There is no actual reduction to practice or clear depiction of what structures or properties constitute a "functional ATM protein". Neither applicant nor the prior art provide a correlation between the structure of ATM and its function. Given the diversity of proteins, variations, fragments and homologs that may be considered as ATM proteins, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection.**

Claims 1-3, 5-7, 9-19 and 21-27 are vague for reciting ATM protein. The metes and bounds of the claimed subject matter are unknown. By reciting broadly, ATM proteins, it is not clear what proteins are to be included in the invention.

Claims 1-3, 5-7, 9-19 and 21-27 are unclear for reciting "functional ATM protein". The specification does not teach what a "functional" ATM protein is. Therefore, it is not clear what criteria exist for functional ATM protein to be included in the invention and the metes and bounds of the claimed invention cannot be established.

Claim 7 is unclear in reciting, "said mammalian cells are HeLa cells" in claim 1. Are the HeLa cells ATM deficient?

Claim 10 recites the limitation "said ATM deficient cells" in 1. There is insufficient antecedent basis for this limitation in the claim. It would be remedial to recite "said ATM deficient mammalian cells".

Claim 17 is unclear for reciting "a high yield" of functional ataxia-telangiectasia. The term "high" is a relative one not defined by the claim, no single set of conditions is recognized by the art as being "high" and because the specification does not provide a standard for ascertaining the requisite degree, the metes and bounds cannot be established.

Claim 22 recites the limitation that the method of isolating ATM protein comprises binding an antibody specific for the FLAG epitope. As this step is in addition to isolation of ATM with an anti-ATM antibody, it is unclear how both antibodies are used in the recited isolation step. The specification does not teach one how to perform isolation of ATM using two different antibodies.

Conclusion

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (703) 605-1207. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Zeta Adams, whose telephone number is (703) 305-3291.

Maria B Marvich, PhD
Examiner
Art Unit 1636

PATENT EXAMINER

August 7, 2003